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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/728,521	12/05/2003	Atul Varadhachary	HO-P02703US2	8270

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EXAMINER	
KAM, CHIH MIN	

ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 12/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/728,521	VARADHACHARY ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7-10,14-20,26-32 and 38-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7-10,14-20,26-32 and 38-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 1, 7-10, 14-20, 26-32 and 38-40 are pending.

Applicants' amendment filed September 26, 2006 is acknowledged. Applicant's response has been fully considered. Claims 1, 26-27, 31, 32 and 38 have been amended. Therefore, claims 1, 7-10, 14-20, 26-32 and 38-40 are examined.

Withdrawn Claim Rejections - 35 USC § 112

2. The previous rejection of claims 1, 7-10, 14-20, 26-32 and 38-40 under 35 U. S. C. 112, first paragraph, scope rejection, is withdrawn in view of applicant's amendment to the claim, and applicants' response at page 6 in the amendment filed September 26, 2006.

Maintained Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Previous rejection of claims 1, 7, 14, 17-19, 26-32 and 38-40 under 35 U.S.C. 103(a) as being unpatentable over by Van Bree *et al.* (WO 01/72322, October 4, 2001) is maintained, and the response to argument is shown below.

Van Bree *et al.* teach human lactoferrin (hLF) can block free LPS and cause them to clear from the body more rapidly, and mask their inflammatory activity; and hLF or LF variants (e.g., N-terminal variants with 1-4 arginine deleted, hLF-2N, hLF-3N, hLF-4N, hLF-5N; pages 4, 5

and 27), which have the biological activities of natural LF (e.g., effective in killing viruses or bacteria), can be used to treat large scale (bacterial) infection, blood-borne infection (sepsis) as well as inflammation resulting from an infection (pages 3-4; page 20, lines 24-29; page 24; claim 1), where the concentration of the polypeptide (LF or LF variant) in the pharmaceutical composition can be at least 1% to 20% by weight (page 24, lines 10-12); and lactoferrin/variant can be administered orally in the form of a solid or solution, and the active components can be encapsulated in gelatin capsules together with inactive ingredients and carriers such as glucose, mannitol or magnesium carbonate (an antacid; claim 14), and the formulated solid or liquid formulations can be in an enteric-coated form (page 26; claims 7, 17-19). Although the reference does not provide a specific example for a method of treating bacteremia, enhancing a mucosal immune response or decreasing mortality using a lactoferrin composition containing the N-terminal variant, it indicates a high dose of hLF or LF variant (e.g., N-terminal variant) having the biological activity of natural LF can be orally administered in the treatment, and hLF or LF variants can be used in treating large scale (bacterial) infection, blood-borne infection (sepsis) as well as inflammation resulting from an infection (see above), which has the same method step as the claimed invention, thus at the time of invention was made, it would have been obvious to one of ordinary skill in the art to orally administer N-terminal variant of LF in the method of treating bacteremia, enhancing a mucosal immune response or decreasing mortality to produce the desired effect as the LF (claims 26-32, 38-40), which results in the claimed invention and was, as a whole, prima facie obvious at the time the claimed invention was made.

Response to Arguments

Applicant indicates to establish a prima facie case for obviousness, all claim limitations must be found or suggested in the references cited or within the general knowledge in the art. The claims have been amended to recite "wherein the N-terminal lactoferrin variant retains the same biological function as full length lactoferrin". Van Bree discloses the N-terminal lactoferrin variants, where the N-terminal amino acids 2-5, which form a basic amino acid cluster, are deleted or mutated to remove the positive charge(s), and Van Bree is quite clear that these variants do not "retains the same biological function as full length lactoferrin (see page 16, lines 14-17). Thus, Van Bree does not disclose or suggest all limitations of the claims as amended. Regarding oral administration, Van Bree teaches oral formulations of lactoferrin (see page 26-27). However, Van Bree also teaches that the "particular form of the composition varies with the intended mode of administration and therapeutic application." There is no suggestion to use oral lactoferrin in the treatment of bacteremia. On the contrary, Van Bree teaches intravenous administration of lactoferrin at high dosages for Bacteremia (see page 3; Examples; page 22, lines 7-12). Taken as a whole, Van Bree cannot be fairly viewed as teaching or suggesting oral administration for bacteremia related sepsis (pages 6-7 of the response).

Applicants' response has been considered, however, the argument is not found persuasive because of the following reasons. Van Bree *et al.* disclose the N-terminal lactoferrin variants can be lactoferrin having 1 to 4 arginine residues from the first cluster (i.e., residues 2-5) deleted or mutated, and the lactoferrin variant can contain one or more arginine residues at N-terminus and have antimicrobial activity (e.g., is effective in killing viruses or bacteria, page 27, lines 9-14).

While the N-terminal variant having one or two arginines deleted may have decreased binding activity toward heparin, lipid A, DNA or human lysozyme as compared to full length lactoferrin as indicated at page 16 of Van Bree's reference, it can still bind to these ligands and have antimicrobial activity, thus the N-terminal lactoferrin variant retains the biological function of the full length lactoferrin, although its activity may be lower than the full length protein, which meets the criteria of the claimed invention. While Van Bree teaches intravenous administration of lactoferrin at high dosages for bacteremia, the reference also teaches oral formulations of lactoferrin and the use of the oral formulation in the treatment of infections of the digestive tract (page 26, line 22+), thus the reference suggests oral administration of the N-terminal lactoferrin variants in the treatment of bacterial infection or sepsis, and which was, as a whole, prima facie obvious at the time the claimed invention was made.

New Claim Rejections-Obviousness Type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 1, 7, 14, 17-19, 26-32 and 38-40 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 16-22, 26-30 and 50-51 of copending Application No. 10/663,258 (based on the amended claims filed

September 26, 2006). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1, 7, 14, 17-19, 26-32 and 38-40 disclose a method of treating bacteremia or sepsis, enhancing a mucosal response in the gastrointestinal tract or decreasing mortality of a subject having bacteremia, comprising the step of administering orally to a subject an effective amount of a lactoferrin composition comprising at least 1% to at least 50% w/w of an N-terminal lactoferrin variant to provide an improvement in the bacteremia of said subject, wherein the N-terminal lactoferrin variant has a deletion, substitution, or combination thereof, of from 1 to 16 N-terminal amino acid residues and wherein the N-terminal lactoferrin variant retains the same biological function as full length lactoferrin; and the specification indicates sepsis or bacteremia may originate anywhere in the body such as surgical wounds or decubitus ulcers (paragraphs [0003] and [0082]). This is an obvious variation in view of claims 16-22, 26-30 and 50-51 in the copending application which disclose a method of treating a wound other than ophthalmic wounds, or enhancing the local or systemic immune system in a subject suffering from a wound by administering to the subject an effective amount of a lactoferrin composition, and the specification indicates a lactoferrin composition can have an N-terminal lactoferrin variant such as N-terminal glycine deleted or substituted or a deletion, substitution, or combination thereof, of from 1 to 16 N-terminal amino acid residues and the N-terminal lactoferrin variant retains the same biological function as full length lactoferrin (paragraphs [0009] and [0048]); and the lactoferrin composition can decrease bacterial infection of the wound (paragraphs [0102]). Both the claims of instant application and the claims of the copending application are directed to a method of treating bacteremia or sepsis, or treating wounds such as wounds causing bacteremia or sepsis by administering a lactoferrin composition

comprising an N-terminal lactoferrin variant. Thus, claims 1, 7, 14, 17-19, 26-32 and 38-40 in present application and claims 16-22, 26-30 and 50-51 in the copending application are obvious variations of a method of treating bacteremia or sepsis, or wounds causing bacteremia or sepsis by administering a lactoferrin composition comprising an N-terminal lactoferrin variant.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

5. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Bragdon can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D.
Primary Patent Examiner

CHIH-MIN KAM
PRIMARY EXAMINER

CMK
November 30, 2006